## REMARKS

The prosecution status of the present application is as follows: the rejections under Section 112, first and second paragraphs, have been withdrawn in view of the Amendment and response filed previously. The only remaining rejections are under Sections 102 and 103, based on the prior art references cited.



This case contains claims 38-45 with the entry of the present Amendment. Claims 1-26 and 34-37 have been canceled without prejudice. The new claims 38-45 are the same except for numbering and dependency as the existing claims indicated below. These claims are simply renumbered to allow the dependent relationships to be readily apparent to the Examiner. Corresponding renumbering is as follows:

Claim 38 is as filed claim 17
Claim 39 is as filed claim 5
Claim 40 is as filed claim 7
Claim 41 is as filed claim 8
Claim 42 is as filed claim 9
Claim 43 is as filed claim 13
Claim 44 is as filed claim 14
Claim 45 is as filed claim 15.

None of the amendments made herein constitutes the addition of new matter.

Claim Rejections under 35 U.S.C. 102:

Claims 1-6. 9-13. 15, 17-19, 22-23, 26, and 34-37 are rejected under 35 U.S.C. 102(b) as allegedly anticipated by Seguin et al. Applicants respectfully traverse this rejection as applied to the current claims.

The Seguin et al. reference does not anticipate the claimed invention. This reference describes an experimental system for determining whether or not mice exposed to mosquitos infected with irradiated *Plasmodium berghei* would be protected against subsequent viable sporozoite challenge. To gain insight into how this protection might occur, a nitric oxide synthase (NOS) inhibitor was added during the challenge step. Based on these experiments, it was concluded that the induction of endogenous NOS enzyme might contribute to the protection against malaria in this animal model.

In contrast, the claimed invention is a method of preventing or treating malarial infection by using an exogenous NO modifying agent in human patients. This invention is based on the inventor's finding that NO production retards parasitic growth and increased levels of NO prevent disease development in non-immunized human patients.



Thus, the distinction between Seguin et al. and the claimed invention are readily apparent. Seguin et al. does not anticipate the claimed invention because it does not disclose all aspects of the invention as currently claimed. The rejection under 35 U.S.C. 102 can be withdrawn.

Seguin et al. is also cited in support of obviousness of claims 8, 14, and 16. This reference cannot provide any suggestion or motivation to make the claimed invention, as is stated therein, "As to whether human hepatocytes exhibit antimalaria activity when stimulated to produce NO, remains to be examined." (See page 353, bottom of the left column). Further, the results obtained from immunized mice of Seguin et al. would not suggest the method of preventing or treating malarial infection in humans by administering an exogenous NO modifying agent.

Claim Rejections under 35 U.S.C. 103:

Claims 1-7, 9-13, 15, 17-26 and 34-37 are rejected under 35 U.S.C. 103 (a) as allegedly unpatentable over Kremsner et al. in view of Liew et al. Applicants respectfully traverse this rejection as applied to the current claims..

Kremsner et al. reports a correlation between endogenous NO levels and severity of the disease in human patients. However, it is not clear whether the NO production is the symptom of the disease pathology or a component of the body's defense mechanism. Thus, it is confusing as to whether high NO levels are beneficial or harmful to the patients. Liew et al. describes the studies involving *Leishmania major*. There is no mention or suggestion of parasites which cause malaria.

Based on the confusing reports of Kremsner and the results on *Leishmania major* by Liew et al, one skilled in the art cannot make the claimed invention. Withdrawal of the rejection as applied to the current claims under 35 U.S.C. (103) is respectfully requested.

Claims 8, 14, and 16 are rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Seguin et al. or Liew et al. in view of Stamler et al. Applicants respectfully tarverse this rejection.

The shortcomings of Sequin et al. has been pointed out above. Liew et al. is not relevant to claims limited to *Plasmodium* infection. Stamler et al. does not provide teachings or suggestions that bridge the gap between Seguin et al. and the invention as currently claimed. The reference merely describes an analytical method to determine plasma levels of free nitric oxide and S-nitrothiols. There is no suggestion or motivation in Stamler et al. for a person of ordinary skill to make and use the claimed invention in combination with Seguin et al.

Based on the foregoing, Applicants submit that the rejection under 35 U.S.C. 103 (a) is not justified and withdrawal of the rejection is respectfully requested.



Conclusion

It is believed that the claims as amended are considered to be in condition for allowance. Careful consideration and passage to issuance is respectfully requested.

This Amendment is accompanied by a Notice of Appeal and the necessary fees. It is believed that this amendment does not necessitate the payment of any (additional) fees under 37 C.F.R. 1.16-1.17. If the amount submitted is incorrect, please deduct from Deposit Account No. 07-1969 the appropriate fee for this submission and any extension of time required.

Respectfully submitted,

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